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Examining the effect of iodized contrast agent of coronary heart angiography in people without thyroid gland disorders

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ABSTRACT

Background: Iodine has a significant effect on thyroid function. A dose of 200 ml of contrast agent contains 35 mg/ml equivalent of 7000 Mg of free iodine and 45 times of the recommended daily dose. This high dose can cause a sudden loss of iodine adjustment, thyroid hormone synthesis, and impair the function of the thyroid gland.

Methods: This study is a cross-sectional study (descriptive-analytical) conducted in census method on 70 patients including 40 men and 30 women referring to Hajar medical education hospital for coronary angiography. Thyroid function tests were given before and after receiving the contrast agent angiography and the changes were finally analyzed.

Results: In this study, after receiving iodinated contrast agent, 8 out of 70 cases studied significantly suffered subclinical hypothyroidism and no one suffered overt hypothyroidism or hypothyroidism. In terms of distribution based on age, there was no significant difference between different age groups in the intensity of hypothyroidism. In terms of gender distribution, from among 70 cases studied, 40 were men, of whom three suffered subclinical hypothyroidisms. Thirty of the subjects were women, of whom five persons suffered subclinical hypothyroidism.

Conclusion: The results show that angiography contrast agent can have effects on the thyroid function of the people with euthyroid, so that out of the 70 patients studied, all of whom were euthyroid, eight patients suffered subclinical hypothyroidism. (p=0.018). Moreover, the age and sex of the participants had no effects on thyroid disorder after receiving angiography contrast agent (P=0.5).

Keywords: Hyperthyroidism, hypothyroidism, contrast agent, angiography, disorders of the thyroid gland

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INTRODUCTION

The fundamental role of iodine in thyroid physiology is well known. This scarce element form 65% of the weight of thyroxine hormone (T4) and 59% of weight of triiodothyronine (T3).

The recommended daily intake of iodine is about 150-250 mcg. Excessive consumption of iodine either using iodine-containing food products or drug products containing iodine will lead to an increased incidence of autoimmune thyroid diseases. Iodized contrast agents are among the most frequently used drugs in modern medicine.[1]

The use of these materials in cardiology and radiology may cause contrast-induced nephropathy, allergic reactions, CVA, and other complications.[2] These materials have a significant effect on thyroid function.[3] The effects of prescribing iodine in patients with thyroid gland disorders are different compared to normal subjects and depend on thyroid gland diseases. For example, iodine therapy in patients with endemic goiter or nodular goiter where the tissue has autonomic function cause hyperthyroid.

Thyrotoxicosis caused by iodine is more common in areas where there is iodine deficiency,4 so that the prevalence of 1-30% of hyperthyroidism after iodine intake has been reported in these areas.[5,6] At the same time, thyrotoxicosis caused by iodine can happen in places where iodine is used sufficiently.[7] Thyrotoxicosis caused by iodine even happens in apparently normal thyroid glands.[8] A dose of 200 ml of contrast agent contains 35 mg/ml equivalent of 7000 Mg of free iodine and 45 times of the recommended daily dose.[8] This high dose can cause a sudden loss of iodine adjustment and thyroid hormone synthesis causing hyperthyroidism, a phenomenon called Jod-Basedow effect.[9] Iodine-induced hyperthyroidism has been reported in patients with thyroid disease, but it mainly occurs in patients with thyroid nodules.[10] More hyperthyroidism is seen following iodine therapy (10-20%) in patients with nodular goiter living in iodine deficient areas.[11] Such patients may have subclinical hyperthyroidism before iodine therapy.[6] Iodine-induced hyperthyroidism is rare in patients without thyroid disease.[12]

In contrast, iodine therapy in patients with autoimmune thyroiditis can lead to hypothyroidism or

aggravating it. Patients at risk of iodine-induced hypothyroidism include: 1) People with chronic autoimmune thyroiditis, 2) patients with Graves' disease who have previously been treated with radioactive iodine or by thyroidectomy, and 3) patients with subacute thyroiditis, postpartum thyroiditis, and painless thyroiditis.[13-15,16] Such patients are unusually sensitive to the inhibitory effects of iodine in organification stage of iodine (Wolff–Chaikoff effect), so that iodine causes the constant activity of iodine/sodium transferor.[13] This continuous activity of the transferor leads to long-term inhibition of the synthesis of thyroid hormones resulting in an increase in TSH concentrations of serum. Hypothyroidism happens in the patients due to impaired escape from Wolff–Chaikoff effect.

Clinical hypothyroidism caused by iodine is similar to other hypothyroidism causes. Hypothyroidism caused by iodine in healthy people normally stops spontaneously within one or two weeks after discontinuation of iodine use.[17-19] Most patients do not need thyroid hormone replacement. Recovery time may be longer in patients who have been exposed to materials that contain iodine not rapidly eliminated from the body (8 weeks or more). In such patients or in cases where the iodine source cannot be eliminated (such as taking amiodarone) thyroid function can easily be normalized with replacement of T4, while the patient is still exposed to iodine. Because of the underlying thyroid disease, patients who risk of temporary iodine-induced hypothyroidism are at risk of permanent hypothyroidism in the future.

Subclinical hypothyroidism is another side effect of subclinical hypothyroidism iodine, where the concentration of serum TSH is higher than normal but T4 serum T3 concentrations are normal. Although there is comprehensive agreement on treatment of patients with subclinical hypothyroidism with serum TSH level higher than 10 mIU/L,[20,23] about the treatment of patients with subclinical hypothyroidism with serum TSH levels between 5-10 mIU/L, there is still no general agreement.[24,25] In Iran, two studies have been conducted in this area. The first study was conducted in Shiraz on 48 patients, who underwent coronary angiography with urografin contrast agent. In that study, it was noted that "coronary angiography with the contrast agent had no significant effect on thyroid function, but in rare cases, in the first few weeks after coronary angiography, it can cause hyperthyroidism.[26] The aim of this study was to find an appropriate solution in the follow-up of patients undergoing coronary angiography to start timely treatment and to prevent complications of thyroid dysfunction in patients with heart diseases, and to suggesting the referral of the patients to specialists in internal medicine, cardiology, and endocrinology after coronary angiography.

METHODS

This study is cross-sectional (descriptive - analytic) conducted to prove hypotheses put forward on patients admitted to cardiac ward of Hajar hospital in Shahrkord. People underwent angiography of coronary artery in angiography unit of Hajar Hospital. All subjects were 70 cases, of whom 40 were male and 30 were female.

Inclusion Criteria

Everyone who underwent coronary angiography with iodine contrast agent were included in the study, and those who did not have conditions for the study were excluded from the study.

Exclusion Criteria

1) Any person who had a personal history of thyroid disease was excluded from the study. 2) People who have abnormal thyroid function tests before angiography were excluded from study. 3) All people who had nodule thyroid or goiter in the thyroid ultrasound performed before were excluded. 4) People using drugs containing iodine such as amiodarone were excluded from the study. 5) People who used drugs affecting thyroid function were excluded as well.

Sample Size and Sampling

In this study, 67 samples are required and about 70 people participated in the study. The sampling was done in census mode where the patients were randomly selected from among those referring to Heart Center of Hajar hospital, Shahrekord who needed for coronary angiography. Variables include age, sex, TSH, FreeT3, and FreeT4.

Data Collection and Tools

In a separate checklist prepared for each patient, thyroid tests result, age, sex, and thyroid sonography results were recorded before angiography, and then the patients underwent coronary angiography after receiving the contrast agent. One month after discharging from the hospital, the patients were contacted to refer to the hospital and do thyroid tests and the results were recorded. In this study, all patients, from October 23, 2013 to January 21, 2014, who had the entry criteria, entered the study. From Everyone who met inclusion criteria were

enrolled. Information form was designed in the form of a questionnaire that did not need validity and reliability.

The sample size according to the statistical counselor was determined 70. Due to exclusion criteria, of the 70 patients, 40 patients were male and 30 were female. First, the complete history of the patient's underlying disease, including thyroid and using iodine-containing drugs were taken and then physical examination was done for thyroid nodules and goiters. If the patient had had the exclusion criteria, he would have been removed from the study; otherwise, they entered the study and thyroid function tests and thyroid sonography were performed. Thyroid tests were TSH, FT4, and FT3. A physician radiologist at the ultrasound center of Hajar hospital performed thyroid ultrasound. Then coronary angiography was being performed and then 4 weeks later the patients were given thyroid function tests, including FT4, FT3 and TSH. The contrast agent used, on average, was 50ml where average iodine in it was 320 mg/ml. Data analysis method was through frequency distribution and percentage for qualitative data, for quantitative data, average standard deviation, and pairwise t-test was used for statistical analysis.

RESULTS

In studies that had been done in the past, in most cases, the patients had suffered hyperthyroidism after receiving contrast. In the study by Martin et al., hyperthyroidism has been shown after the use of contrast agents.[27] In another study, only two patients out of 788 patients of hyperthyroidism iodine deficiency suffered hyperthyroidism 12 weeks after angiography, and so in this study, it was found that in adult patients without morphological changes of the thyroid gland and thyroid function, thyroid test is a single dose and high contrast agent are safe.[28] In one study where patients underwent IVP, T4 increased, TSH decreased, but T3 did not change. Two patients suffered hyperthyroid and 1 suffered AF.[29] In Iran, two studies have been conducted in this area. The first study was conducted in Shiraz on 48 patients, who underwent coronary angiography with urografin contrast agent. In that study, it was noted that coronary angiography with the contrast agent had no significant effect on thyroid function, but in rare cases, in the first few weeks after coronary angiography, it can cause hyperthyroidism.[26] In another study, conducted in Kermanshah, it was noted that coronary angiography with iodized contrast agent has a significant effect on thyroid function test, and after the first few weeks after coronary angiography, it may cause hyperthyroid. This side effect in the elderly and people who have coronary artery disease can be dangerous.[30]

In 2013, a study was conducted on 101 patients with euthyroid in Turkey who underwent coronary angiography. The results of this study showed that TSH levels of patients significantly decreased during the fourth and eighth weeks after treatment. In this study, all the patients, before angiography, underwent thyroid and thyroid sonography, so that all normal patients are completely enter the study. According to the study, the risk of developing subclinical hypothyroidism after receiving the contrast agent containing iodine has been proposed.[31]

Based on Paired Samples Correlations, the comparison between the thyroid hormones before and after angiography in men is as follows (Fig. 1).

- There is a significant correlation between T3 before and after coronary angiography (p = 0.014).
- There is no significant correlation between T4 before and after coronary angiography.
- There is a significant correlation between TSH value before and after coronary angiography with correlation coefficient of 0.67.

Based on these data and based on Paired Samples Correlations, there is a significant relationship in comparison between thyroid hormones before and after angiography, according to Table 2 separately for women groups, T3, T4 and TSH before and after coronary angiography.

In this study, subjects were divided into three age groups: the age group 20-39, 40-59, and 60 years of age years (Fig. 3). Based on Paired Samples Correlations test, there is a correlation between thyroid hormones levels before and after angiography according to Table (3) separately in the age group 20-39 years in T3 and TSH, before and after coronary angiography, which is meaningful. 2. There is a correlation between T4 before and after angiography with correlation coefficient 0.27 that is not significant (p=0.119).

Based on Paired Samples Correlations test, there is a correlation between thyroid hormones levels before and after angiography according to Table 4 separately in the age group 20-39 in T3, with correlation coefficient 0.75, which is not

Table 1 **Thyroid hormone levels before and after coronary angiography in men**

	Before angiography	After angiography	Correlation coefficient	P
T3	0.4 ± 1.29	0.4 ± 1.4	0.38	0.014
T4	1.12± 7.22	1.8 ± 7.86	0.26	0.105
TSH	2.01± 2.63	2.16± 2.25	0.67	0.001

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Table 2 Thyroid hormone levels before and after coronary angiography in women

	Before angiography	After angiography	Correlation coefficient	P
T3	0.38 ±1.36	0.39 ±1.38	0.57	0.001
T4	1.19± 7.78	1.27± 7.21	0.37	0.042
TSH	1.46± 2.3	2.02± 2.856	0.72	0.001

Table 3 Thyroid hormone levels before and after coronary angiography in the age group 20-39

	Before angiography	After angiography	Correlation coefficient	P
T3	0.37 ± 1.26	0.39 ± 1.34	0.75	0.001
T4	1.52± 7.9	1.23± 7.21	0.27	0.119
TSH	2.51± 2.28	2.03± 2.62	0.79	0.001

Table 4 Thyroid hormone levels before and after coronary angiography in the age group 40-59

	Before angiography	After angiography	Correlation coefficient	P
T3	0.37 ± 1.25	0.4 ± 1.34	0.75	0.119
T4	1.52± 7.9	1.23± 7.39	0.27	0.001
TSH	1.51± 2.28	2.03± 2.62	0.79	0.001

Table 5 Thyroid hormone levels before and after coronary angiography in age group over 60

	Before angiography	After angiography	Correlation coefficient	P
T3	0.4 ± 1.38	0.4 ± 1.45	0.26	0.387
T4	1.17± 7.58	1.7 ± 8.09	0.36	0.038
TSH	2.08± 2.76	2.04± 2.81	0.6	0.001

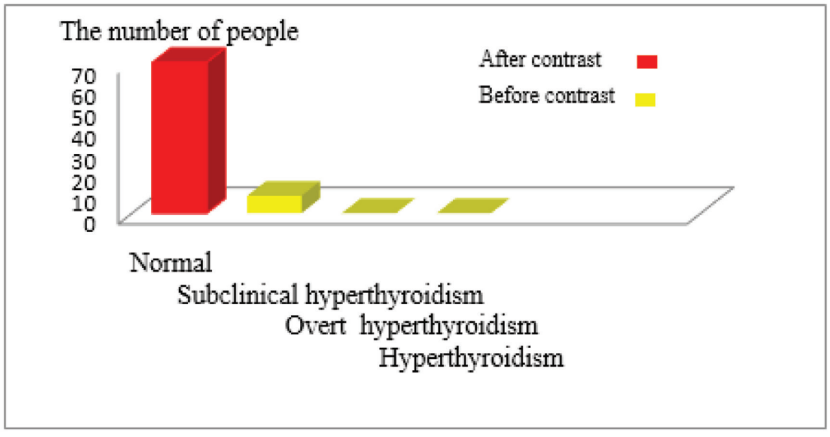

Figure 1 The effect of iodized contrast agent of coronary angiography on the thyroid function in people without thyroid gland disorder

meaningful (p=0.119). 2. There is a significant correlation between T4, TSH before and after angiography in the age group 40-59.

Based on Paired Samples Correlations test, there is a correlation between thyroid hormones levels before and after angiography according to Table 5 separately in the age group 60 in T3, with correlation coefficient 0.16, which is not meaningful. There is a significant correlation between T4, TSH before and after angiography.

The effect of coronary angiography iodized contrast agent on thyroid function in people without thyroid gland disorders, regardless of age and gender, is obtained as follows. According to Figure 1, all people without thyroid gland disorder that met the inclusion criteria were 70, of whom 8 patients suffered subclinical hypothyroidism after receiving iodized contrast agent and no patient developed hypothyroidism or overt hyperthyroidism (P=0.018).

In terms of gender distribution from among the 70 cases studied, 40 were male, of whom after receiving the iodinated contrast agent, no one suffered overt hypothyroidism or hyperthyroidism, but three patients suffered subclinical hypothyroidism. Thirty persons of the subjects were women, of whom after receiving iodinated contrast agent, no one suffered overt hypothyroidism or hypothyroidism, but five persons suffered subclinical hypothyroidism (Figure 2). Based on Independent Sample Test, in terms of suffering hypothyroid, there is no difference between male and female gender in hypothyroid (P=0.167).

In terms of distribution of age, 70 studied patients were divided into three age groups. In the age group 20-39, the number of people was three, none of whom suffered thyroid disorder after receiving iodinated contrast agent. In the age group 40-59, the number was 34 that after receiving iodinated contrast agent no one suffered overt hyperthyroidism and hypothyroidism, but four people suffered subclinical hypothyroidism.

The number of people in age group 60 and over was 33 people that after receiving iodinated contrast agent, no patient suffered overt hyperthyroidism and hypothyroidism, but four people suffered subclinical hypothyroidism (Figure 3). Based on analysis of variance (One Way Anova), in terms of suffering hypothyroid, there was no significant difference between three age groups (P=0.5).

CONCLUSION

In this study that was conducted in Shahrekord (Chaharmahaland Bakhtiari Province) on 70 people, no cases had hyperthyroidism up to four

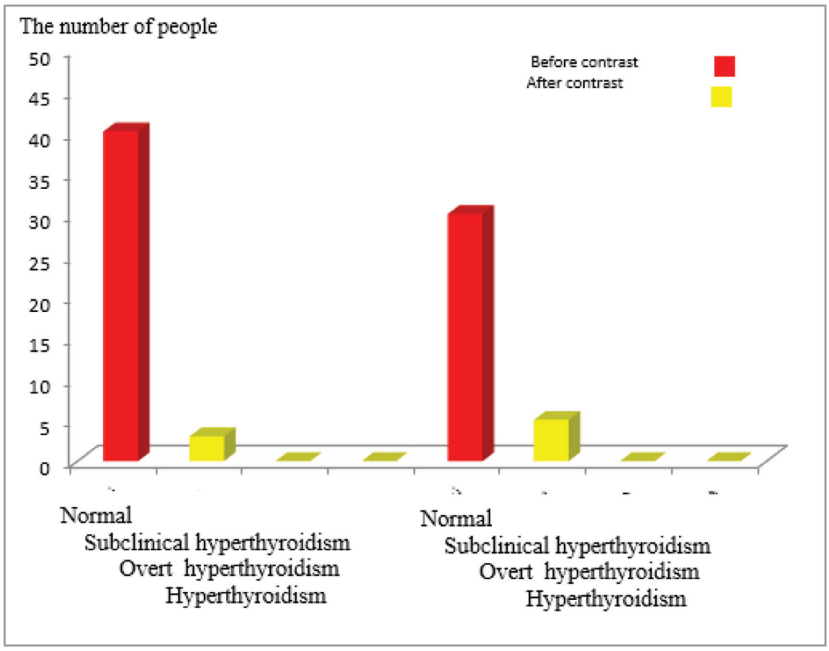

Figure 2 The effect of gender on iodized contrast agent of coronary angiography on the thyroid function in people without thyroid gland disorder

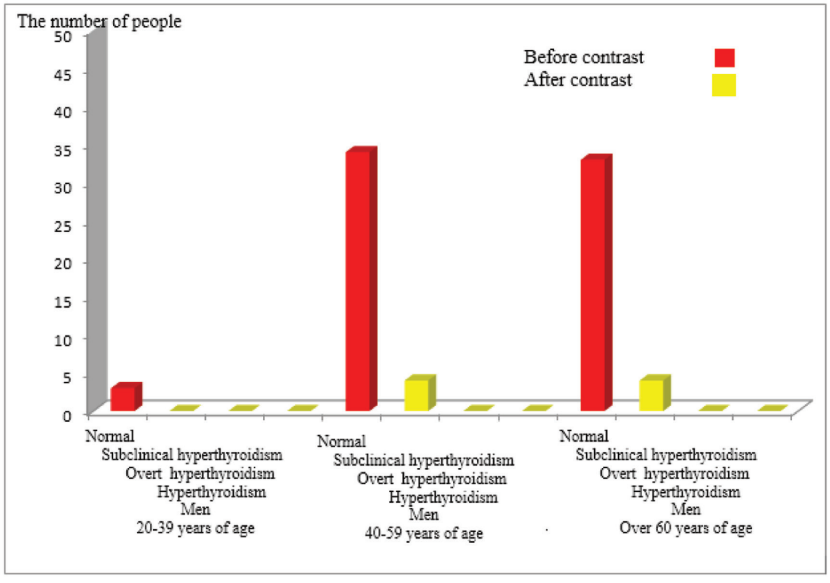

Figure 3 The effect of age on the effectiveness of coronary angiography iodine-contrast agent on the thyroid function in people without thyroid gland disorders

weeks after coronary angiography in euthyroid individuals without thyroid disease. In eight cases, there was TSH increase without changes at T3 and T4; in fact, these patients suffered subclinical hypothyroidism, and no cases of overt hypothyroidism were observed. Overall, of 70 patients studied all of whom were euthyroid without thyroid construction diseases, and only eight patients suffered subclinical hypothyroidism. In terms of impact of gender on the effect of iodized contrast agent of coronary angiography on thyroid function, from among 40 men, after subclinical hypothyroidism angiography, three patients suffered subclinical hypothyroidism.

From among 30 women, after subclinical hypothyroidism angiography, five patients suffered subclinical hypothyroidism. From among these people, neither in women nor in men, there were cases of overt hypothyroidism or hyperthyroidism. According to independent sample test, gender has no role in suffering hypothyroid between women and men (p=0.167). In terms of changes in thyroid function tests separately for men and women in age groups, it can be said that between men, there was no significant relationship between T4 changes before and after angiography, (P=0.105), but changes in other tests after coronary angiography compared to before had significant and growing changes.

Among women, all the tests showed significant increase compared to before (P<0.05), but given our analysis of the thyroid tests is in form of combined analytical tests T3, T4 and TSH are generally not significant. People in the age group 20-39are three people that after receiving the contrast agent, none suffered impairment in thyroid function. In other words, no patient suffered hypothyroidism or thyrotoxicosis after 4 weeks. People in the age group 40-59who were 34 patients, after receiving contrast agent, only four people suffered from subclinical hypothyroidism (SCH). In people in the age group 60 or more who were 33 subjects, after receiving contrast agent, four people developed subclinical hypothyroidism (SCH). In none of the age groups, cases of overt hypothyroidism (OH) and hyperthyroidism were observed. Based on analysis of variance (One Way Anova), in comparison between three age groups, there was no significant difference in the presence of hypothyroidism (p=0.5). Therefore, it can be concluded that age had no effect on hypothyroid of patients. The impact of age on the effect of contrast agent on thyroid function tests showed no changes only in the age group 20-39between T4 before and after the test (0.119), and other related variables had changes in form of increasing. In the group 40-59, except for T3 the rest of the data were significantly correlated (P<0.018). In the analysis of the results, in every thyroid test, each thyroid test changes after angiography compared to before, it can be seen that although some of these changes are significant, they have no effect on the overall results of the study, and have no clinical value.

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